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1200 G Street NW, Suite 400
Washington, DC 20005-3814
Tel: 202 783 8700
Fax: 202 783 8750
www.AdvaMed.org



AdvaMed's Written Testimony
before
FDA's
Transmissible Spongiform Encephalopathies
Advisory Committee

by

Peter A. Burke, Ph.D.
Vice President & Chief Technology Officer
STERIS Corporation

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Good morning. My name is Peter Burke. I am Vice President and Chief Technology Officer for STERIS Corporation. I am here today as the spokesperson for the Advanced Medical Technology Association, more commonly known as AdvaMed. AdvaMed is the largest medical technology association in the world, representing more than 1,100 innovators and manufacturers of medical devices, diagnostic products, and medical information systems. Many of these products are manufactured from source materials derived from ruminants, sourced from countries around the world. Thus, the potential risk of TSE contamination associated with medical devices is an important issue for AdvaMed member companies.

In fact, manufacturers consider source control to be the most effective safety control measure available to mitigate any potential risk of TSE introduction. AdvaMed members made a recommendation to FDA last year that the agency adopt a flexible approach to allow device manufacturers to determine measures of theoretical risks for medical devices. Source control was the central pillar of that flexible approach, and we believe that this is a highly effective step in preventing the contamination of medical devices and manufacturing facilities.

However, in order to be prepared for any potential risk of TSE contamination, this committee, CDC, FDA and USDA all face the monumental task of developing criteria for designing and validating studies intended to evaluate the effectiveness of TSE decontamination methods. We commend this effort and believe that it is necessary to ensure the continued availability of safely reprocessed medical devices and medical devices containing animal derived materials in an environment where the number of TSE free countries is declining, and can change overnight.

In the United States there are currently no approved guidelines for decontaminating medical devices that might potentially be contaminated with prions, considered the causative agent of TSEs. Prions are considered highly resistant to the routine methods of decontamination and sterilization currently accepted for medical device processing. Thus removal of prions presents a significant challenge to manufacturers.

General Decontamination Methods

The challenge of decontaminating medical devices and manufacturing facilities that may be potentially contaminated with prions has several components, and it is important to consider the body of experimental work that has been done. To date, in experimental studies, no single decontamination method has been shown to be 100% effective against prions. Therefore, a combination of methods is generally recommended.

Current decontamination methods are based on recommendations from the World Health Organization (WHO). The WHO recommendations are based on a review of the current published literature. The effectiveness of these methods is difficult to assess. There are no standardized methods to evaluate the effectiveness of any given decontamination procedure for prions.

Based on our review of the literature used by WHO, it is difficult to determine which decontamination methods are truly effective. It is also difficult to compare studies, as a variety of prion proteins (e.g., scrapie, BSE or CJD isolates) were used. In addition, the studies employed different preparation methods (e.g., purified or non-purified, homogenates or intact brain) and used different test methods (e.g., suspension or carrier tests). Evaluation of the decontamination methods also failed to consider the antimicrobial effects of biocides and physical/biocidal processes, which vary based on the process parameters (e.g., active concentration and temperature). Consequently, the results of many of the studies cited in the literature may not be reproducible.

In the United States, the Healthcare Infection Control and Practices Advisory Committee (HICPAC) of the Center for Disease Control & Prevention developed draft guidelines as part of their Guideline for Disinfection and Sterilization in Healthcare Facilities. These guidelines, which are yet to be approved, are also based on the WHO recommendations. As a result, they too fail to include a standardized method of evaluation.

If we are to answer the question of which method should be employed, we must first have a mechanism to compare the available methods. In addition, the panel must recognize that, in the current absence of globally accepted standardized methods for evaluation, additional studies would likely be necessary to achieve more definitive global guidelines. We believe that today's proceedings are an important first step to doing so.

Facility Issues

Currently, contamination of manufacturing facilities is a theoretical risk. If products were to be contaminated with TSE agents, the decontamination of manufacturing facilities, in order to limit the potential for cross contamination of medical devices or other regulated products, presents manufacturers with a considerable logistical challenge. Since to date, no single method of decontamination has been proven 100% effective against prions, any FDA requirements to decontaminate manufacturing equipment and facilities should take into consideration the potential risk of cross contamination from contaminated materials and the potential for transmission of a TSE based on patient or user contact. Decontamination methods should be based on this risk assessment and whether the process selected has been established as being effective under the specific use conditions.

If effective methods are identified, other considerations would come into play. For example, would the method be compatible with medical device production and manufacturing equipment? Identified decontamination methods should be compatible with the surfaces being treated to minimize damage to manufacturing equipment. How frequently should one apply such methods following each manufacturing run, after every single lot, or at some other determined frequency? How does the implementation of prion decontamination methods impact equipment qualifications and process validations? Will it be necessary to re-qualify all manufacturing lines? The answers to these questions are important, as they will impact the day-to-day manufacturing of medical devices. There is the potential that any new

and possibly onerous requirements on medical technology manufacturers could limit manufacturers' ability to provide needed quantities of life-saving medical products in a timely way to the patients who need them. AdvaMed strongly encourages that any discussion about development of standardized decontamination methodologies to reduce any perceived risk of BSE cross-contamination take these considerations into account.

Furthermore it may be appropriate to consider alternative approaches for those medical technologies that do not come into human or animal contact. Material control of these products through the use of standard quality systems must not be overlooked as an alternative approach to the implementation of any new decontamination procedures. Material control processes for these products already address the identity, traceability, handling, and disposal of materials within their quality systems. Assurances provided by these systems provide a viable alternative to facility decontamination.

Device Issues

Another component of the decontamination challenge is the impact of various decontamination methods on a device. Can the device withstand being subjected to new and potentially rigorous decontamination and processes, above and beyond its current regimen of safety and sterility processes, and still retain performance integrity to remain safe and effective for its intended use? The answer is complex. Several of the current WHO recommendations for medical device reprocessing will cause severe damage to common medical device surfaces. For example, WHO's recommendation for using 1 N NaOH can severely damage to aluminum and stainless steel components and when used in an autoclave could severely damage the internal chamber of the autoclave. The impact of current decontamination processes on devices and in vitro diagnostic devices (IVD) is unclear. It is likely they would not stand up to these extreme decontamination procedures.

Most IVDs contain some sort of animal-derived materials, much of which is derived from ruminants. These materials are key to the performance of the IVD. In many cases, the materials have been developed to yield certain unique performance characteristics. If required, decontamination processes could literally destroy or inactivate this ingredient in many IVDs. Since these devices are not intended to contact either the human body or animals, requirements for decontamination procedures would be superfluous.

Where decontamination is a viable option, the method of decontamination is an important consideration. The method used must be compatible with the material of the device. When a combination of procedures is required to decontaminate a device, the effect that each one has individually and in combination must be assessed. The decontamination process must not render the device unsafe for its intended use. We encourage the Advisory Panel to take into account the unique concerns associated with the decontamination of medical devices whose original design never contemplated cleaning and sterilization after exposure to potential TSE causative agents.